REMARKS

Claims 1-14 and 16-47 are active in the present application.

Applicants wish to remind the Examiner that Claim 21 is still pending. Although not explicitly restated in paper number 20, Claim 21 has been indicated as being allowed (see paper number 17, page 4, line 18). Acknowledgment of the allowed status of Claim 21 is requested.

The rejection of Claims 1-14, 16-20, and 22-38 under 35 U.S.C. §112, first paragraph, is traversed.

At the outset, Applicants again note that MPEP §707.07(f) states:

> "Where the applicant traverses any rejection, the examiner should, if he or she repeats the rejection, take note of the applicant's argument and answer the substance of it."

In maintaining the current rejection, the Examiner fails to note the essence of Applicant's argument, much less answer the substance of it. Clearly if the Examiner had attempted to do the same, the Examiner would have appreciated that the Board has already addressed the Examiner's concerns in Ex parte Breuer, 1 USPQ2d 1906 (Bd. Pat. App. & Inter. 1986), which was provided to the Examiner with the responses filed on July 25, 2003 and February 19, 2003 (a copy of which is again **submitted herewith**).

It appears that the Examiner has based this ground of rejection largely on the following two points: (1) the "limited number" of exemplified N-containing cycloalkyls at position R^1, and (2) the "limited number" of exemplified compounds demonstrating inhibition of platelet aggregation.

In regard to the first point, Applicants wish to bring the Examiner's attention the

definition on page 28, lines 26-31 of the specification, which unequivocally defines the meaning of the term "N-containing cyclo(lower)alkyl." Applicants further note that the skilled artisan would readily appreciate the scope of permissible N-containing cycloalkyls, as well as how to make and use the same without undue experimentation.

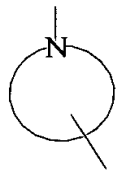
In maintaining the rejection, the Examiner states, "there is insufficient exemplification to show that all of the iring [*sic*, ring] systems could be attained synthetically as claimed." Applicants must admit that they are mystified by this assertion by the Examiner, especially in view of the ***nearly 250 examples*** provided in the present application, which even a cursory review evinces that the exemplified compounds exemplify, minimally, an R^1 of a substituted or unsubstituted piperidyl combined the following N-containing heterocycles: piperidyl, morpholinyl, pyrrolidinyl, and quinolinyl. Moreover, the specification clearly establishes that suitable -containing cyclo(lower)alkyls include: azetidinyl, pyrrolidinyl, piperidyl, and piperazinyl (see page 28, line 30).

Turning to the second point above, Applicants vehemently disagree with the Examiner's assertion in that there is no requirement for Applicants to provide any working example (MPEP §2164.02). The proper standard for examination is whether the artisan can make and use the claimed invention without undue experimentation (MPEP § 2164.01). In view of the disclosure provided in the present application, Applicants submit that a person possessing a technician's level of skill would be able to follow the protocol on pages 46 and 47 to determine the effectiveness of a compound falling within the scope of the claims for treatment of diseases caused by thrombus formation and/or inhibition of platelet aggregation.

Applicants once again wish to draw the Examiner's attention to the attached copy of Ex parte Breuer, 1 USPQ2d 1906 (Bd. Pat. App. & Inter. 1986), reviewing an Examiner's decision to reject claims under 35 U.S.C. § 112, first and second paragraph, for the alleged

lack of enablement and indefiniteness of the terms "heterocycle" and "substituted" (id. at 1906-1907). In Breuer, the application in question disclosed how to make and use the claimed compounds, including 50 examples of the claimed compounds and a definition of both the terms "heterocycle" and "substituted" (id.). The U.S. Board of Patent Appeals reversed the Examiner's rejection based on the above facts in Ex parte Breuer found sufficient disclosure to enable a person having ordinary skill to practice the claimed invention without undue experimentation (id. at 1907).

Like Ex parte Breuer, the present specification provides a full definition of the term "heterocyclic" and/or derivatives of the term. Further, the present specification provides a full definition of the term "substituent" and/or derivatives of the term. Specifically, at page 14, line 1 to page 29, line 12, the Applicants fully disclose the acceptable variants of the R^1 (especially, N-containing cycloalkyl groups), R^2, R^3, A^1, A^2, and A^3 substituents, as well as the heterocyclic substituent of formula:



for use in the present invention. Also like Ex parte Breuer, the present specification discloses how to make the claimed compounds (page 4, line 21 to page 13, line 13 and at page 36, line 15 to page 47, line 24) and further provides ***nearly 250 examples*** of compounds having "heterocyclic" groups and "substituents" (see page 50, line 24 to page 165, line 11).

The Examiner asserts that "undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level

of predictability in the art of the invention, and the poor amount of direction provided by the inventor" (paper number 20, page 4, lines 13-16). In Ex parte Breuer the Board did not find a patent including 50 examples of the claimed compounds to require undue experimentation or to have provided a "poor amount of direction." Despite the precedent set in Ex parte Breuer, the Examiner concludes: "Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application" (paper number 20, page 4, lines 16-17).

However, in view of the Board's holding and their status as a *precedential* authority, Applicants ask how the Examiner can hold an application that provides ***nearly 250 examples*** of the claimed compound not to be enabled? Therefore, like in Ex parte Breuer, the Examiner's rejection should be withdrawn.

Moreover, even in the absence of the clear precedent set by the Board in Ex parte Breuer, Applicants submit that the present application is enabled in yet a completely different manner.

MPEP §2164.04 states:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, *unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.*

Not only do the Applicants provide adequate disclosure to fully enable the skilled artisan to make the claimed compounds (see discussion of Examiner's point (1) above), Applicants have provided a test to enable the skilled artisan to assess the efficacy of the compounds made thereby (page 47, line 31 to page 48, line 17). Applicants also disclose preferred uses of the compounds of the present invention (page 48, line 19 to page 50, line 1).

In addition to the extensive disclosure provided by the present application, the

numerous examples provided by the present application, and the Board's decision in Breuer, the Examiner has not provided any reason whatsoever to "doubt the objective truth of the statements contained therein which must be relied on for enabling support." Accordingly, this rejection is also unsustainable since the *Examiner has not met the burden* necessary to refute the adequacy of the present disclosure.

Further regarding Claim 17, it appears that the Examiner has merely reasserted the rejection under 35 U.S.C. §112, first paragraph, *in toto*, without regard for breadth of the rejection. The Examiner has remained silent with respect to this ground of rejection and Applicants argument thereto. In Applicants' response of June 12, 2002, Applicants pointed to page 1, line 21 to page 2, line 10, which sets forth that platelet aggregation and thrombus formation are widely recognized to be causative of a series of disorders including, restenosis or reocclusion; the thrombus formation in case of vascular surgery, valve replacement, extracorporeal circulation or transplantation; disseminated intravascular coagulation; thrombotic thrombocytopenic; essential thrombocytosis; and inflammation. Accordingly, treatment of these disorders would be well within the purview of the skilled artisan with the present application in hand.

As is clearly evident above, Applicants have adequately enabled the present invention and have disclosed how to make and use the compounds of the present invention thereby placing these compounds and their uses in the possession of the skilled artisan without undue experimentation. Therefore, with the present specification in hand, the skilled artisan would require nothing more than *routine* skill to realize the scope of the presently claimed invention, obtain the compounds of the present invention, practice the method of the present invention, and to assess the efficacy of the presently claimed compounds. The Examiner has not offered any evidence to refute these asserted facts, but rather has elected to merely recapitulate the

previous rejections without providing any further evidence to support the rejection other than unsupported statements that fail to compensate for the overwhelming support for enablement of the present invention as stated above.

For all the foregoing reasons, Applicants request withdrawal of this ground of rejection.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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